MONOGRAPH

PAMIDRONATE

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Prescribing Calcium/Vitamin D Dosing	Monitoring

DRUG CLASS

Pamidronate is a bisphosphonate.[1]

INDICATIONS AND RESTRICTIONS[2, 3]

Indications **not listed** below will require individual patient application (IPA) approval from the Drug and Therapeutics Committee (DTC):

- PBS-listed indications.
- Primary osteoporosis (osteogenesis imperfecta).
- Secondary osteoporosis or osteopenia.
- Refractory hypercalcaemia.
- Idiopathic avascular necrosis or Legge-Calve-Perthes disease.

CONTRAINDICATIONS

- Hypersensitivity to pamidronate or any component of the formulation.[4]
- Calcium and 25-Hydroxy-Vitamin D level must be within normal limit prior to commencing pamidronate (except when used for treatment of hypercalcaemia).[3]
- Pre-existing hypocalcaemia.[5]

- Active rickets associated with mineral deficits.[3]
- Pregnancy – patients with childbearing potential should be tested prior to each infusion. Patients/guardians must be advised of contraception requirement if applicable.[5]

PRECAUTIONS

- Patients with significant co-morbidities or risk factors for hypocalcaemia may be admitted for up to three days for treatment and observation for their first infusion, or subsequent infusions if clinically indicated.
- Dehydration – correct prior to commencing pamidronate and maintain adequate urine output during treatment of hypercalcaemia.[5]
- Concurrent use with other nephrotoxic drugs.[5]
- Invasive dental procedures or pre-existing major dental complications – increased risk of osteonecrosis of the jaw (ONJ).[5]

FORMULATIONS

90mg/10mL vial.[6]

DOSAGE & DOSAGE ADJUSTMENTS

Dosage and frequency are dependent on the indication and may deviate from usual recommendations at the discretion of the treating consultant.

Dosing in Overweight and Obese Children: Dose based on patient's ideal body weight.

Primary osteoporosis

- **Bisphosphonate naïve** patient: Consider giving a lower first dose (0.5 mg/kg) to minimise acute phase reactions and hypocalcaemia.[3]
- **[First 12 months of pamidronate therapy]:**
  9 mg/kg/**YEAR** in 4 – 6 divided doses (max 60 mg/dose).[3]
- Repeat DXA (Dual Energy X-ray Absorptiometry) scan after 12 months of therapy then continue treatment as below[3]:
  - Total BMD Z score ≤ -2.0 ➜ continue same annual dose.
  - Total BMD Z score ≥ -2.0 but <0 ➜ 4.5 mg/kg/**YEAR** in 4 – 6 divided doses (max 60mg/dose)
  - Total BMD Z score > 0 ➜ 3 mg/kg/**YEAR** in 2 divided doses (max 60 mg/dose), if maintenance therapy indicated.

Spine or TBLH (total body less head) BMD rather than total BMD, is typically assessed in paediatrics and adolescents.[7]

Secondary osteoporosis[3]

- **[First 12 – 24 months of pamidronate therapy]:**
  9 mg/kg/**YEAR**, in 4 – 6 divided doses (max 60 mg/dose).
  - ➢ Repeat DXA (Dual Energy X-ray Absorptiometry) scan after 12 months and review therapy
- Maintenance therapy after 2 years, if indicated:
  3 mg/kg/**YEAR**, in 2 divided doses (max 60 mg/dose).

Idiopathic avascular necrosis (AVN), Legg-Calvé-Perthes disease[8, 9]

- 1 mg/kg (max 60 mg) every 1 – 2 months.

Refractory hypercalcaemia[3, 4]

- **Usual dose:** 0.25 – 1 mg/kg/dose (max 90 mg).
- **Severe/life-threatening hypercalcaemia:** 1.5 – 2 mg/kg/dose (max 90 mg).
- Dose may be repeated after at least 24 hours from initial dose. Consider other management options if hypercalcaemia persists after two doses.

Renal impairment:

- eGFR calculator
- Dosage adjustment may be necessary for pamidronate use in renal impairment.[4]

Hepatic impairment: No data available. Not hepatically metabolised.[4]

PRESCRIBING[3]

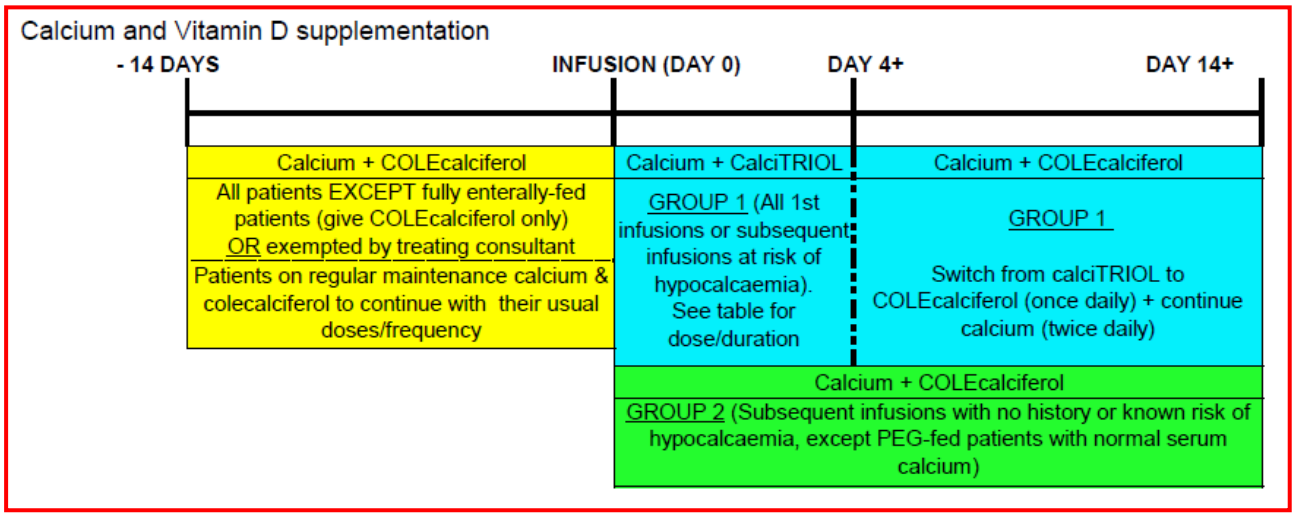
- Prescribe paracetamol or ibuprofen (as required) on the paediatric Hospital Medication Chart (pHMC) to treat acute phase reaction symptoms (flu-like symptoms).
- Prescribe pamidronate infusion on MR828 IV Fluid Therapy Order sheet.

The remaining information in this section only applies to patients receiving pamidronate for indications other than hypercalcaemia.

- *Patients at low risk of hypocalcaemia may, at the treating consultant's discretion, not require pre- or post-infusion calcium and/or vitamin D (e.g. rheumatology patients using bisphosphonates for AVN with no known co-morbidities that may increase their risk of hypocalcaemia).*

COLEcalciferol and **calciTRIOL** are not equivalent. Calcitriol is the active form of vitamin D.
Patients **SHOULD NOT** be taking both forms concurrently
(i.e. withhold colecalciferol when taking calcitriol).

Calcium doses may be rounded to the nearest 150 mg (quarter of a 600 mg tablet) or 125 mg (quarter of a 500 mg tablet), if a tablet is preferred.



PRE–infusion calcium and COLEcalciferol supplementation

Patients should receive calcium and colecalciferol supplementation prior to pamidronate infusion *(see exceptions below)*

- Non-ambulatory fully enterally–fed patients with normal calcium levels do not require additional pre-infusion calcium supplementation but should be prescribed COLEcalciferol.
- Patients receiving ongoing (regular) calcium and vitamin D supplements, with normal serum calcium and vitamin D levels do not require additional pre-infusion supplementation (i.e. continue on their usual maintenance dose and frequency).
- Patients with normal serum calcium / vitamin D levels and at low risk of bisphosphonate-related hypocalcaemia may be exempted from pre-infusion calcium / colecalciferol supplementation at the treating consultant's discretion.
- Recommended dose and duration:

Drug	Dose (enteral)	Commence
Elemental calcium	20 mg/kg (max 600 mg) TWICE daily	14 days pre-infusion
COLEcalciferol (Vitamin D_3)	Refer to Colecalciferol guideline	14 days pre-infusion

- Consider using combination product containing elemental calcium 600 mg + colecalciferol 500 units/tablet if appropriate. ***(Preferred formulation for patients under the care of Paediatric Rehabilitation team)***.

POST–infusion calcium and vitamin D supplementation (Note: Group 1 vs Group 2)

- Intravenous calcium infusion may be necessary in patients with severe symptomatic hypocalcaemia. Refer to calcium monograph.
- Patients with normal serum calcium / vitamin D levels and are at low risk of bisphosphonate-related hypocalcaemia may be exempted from post-infusion calcium / colecalciferol supplementation at the treating consultant's discretion.

Group 1: ALL FIRST infusions or all subsequent infusions at risk of hypocalcaemia)

- Patients with history of pamidronate or other bisphosphonate-induced hypocalcaemia should be managed as post-first infusion (i.e. should be prescribed calcium and calcitriol following subsequent infusions).

- Following treatment with calciTRIOL, patients should step down to COLEcalciferol to complete at least 14 days in total of vitamin D therapy post-infusion.
  - Recommended dose and minimum duration:

Serum calcium level (24hrs post-infusion)	Drug	Dose (enteral)	Duration
≥ 2 mmol/L	Elemental calcium	20 mg/kg (max 1 g) **TWICE daily**	14 days
	CalciTRIOL	0.25 microg**/DOSE** (NOT per kg) **TWICE daily**	≥ 4 days, then step down to COLEcalciferol **once daily**
< 2 mmol/L	Elemental calcium	20 mg/kg (max 1 g) **THREE times daily**	Until serum calcium ≥ 2 mmol/L, then reduce to **twice daily**
	CalciTRIOL	0.25 microg**/DOSE** (NOT per kg) **THREE times daily**	Until serum calcium ≥ 2 mmol/L, then step down to COLEcalciferol **once daily**
It is recommended that patients complete a total of 14 days calcium & vitamin D therapy. Exact duration of treatment to be determined by treating consultant.			

Group 2: SUBSEQUENT infusions (no history or known risk of hypocalcaemia):

- Patients who have previously tolerated pamidronate infusion without hypocalcaemia *(see exception below)* should be prescribed calcium and COLEcalciferol for at least 14 days post-infusion.
  - Non-ambulatory fully enterally–fed patients with normal calcium levels do not require additional post–infusion calcium supplementation.

- Recommended dose:

Drug	Dose (enteral)	Duration
Elemental calcium	20 mg/kg (max 600 mg) **TWICE daily**	14 days post-infusion
COLEcalciferol (Vitamin D_3)	Refer to Colecalciferol guideline	14 days post-infusion

- Consider using combination product containing elemental calcium 600 mg+colecalciferol 500 units/tablet if appropriate. ***(Preferred formulation for patients under the care of Paediatric Rehabilitation team)***.

ADMINISTRATION

- During pharmacy operating hours, pamidronate infusion is prepared by PCH Pharmacy Compounding Services (PCS).
- Dilute to a concentration of 0.36 mg/mL or less with compatible fluid and infuse over 2 to 4 hours.[10] Longer infusion times reduces risk of nephrotoxicity.[10]
- Ensure patient is adequately hydrated prior to, during and after the infusion.[5, 10]

COMPATIBILITY

Compatible fluids: Sodium chloride 0.9%, glucose 5%.[10]

MONITORING[3, 5]

- **With each infusion** – Baseline temperature, pulse and respiratory rate (TPR), blood pressure; repeat every 30 minutes until 1 – 2 hours post-infusion. Frequency of monitoring for inpatients may then be reduced to standard frequency.
- Monitor serum or ionised calcium levels.

Recommended additional monitoring for all indications **other than hypercalcaemia**:

- **Monitoring requirements may vary at the treating consultant's discretion.**
- In the presence of renal disease and impaired creatinine production / clearance, measurement of glomerular filtration rate (GFR) using radio-contrast may be necessary. Discuss with an endocrinologist.
- **WORKUP prior to FIRST infusion**– serum or ionised calcium (blood gas), phosphate, magnesium, full blood count, UEC (urea, electrolytes and creatinine), renal function, renal ultrasound, alkaline phosphatase (ALP), serum 25-hydroxy vitamin D, parathyroid hormone, dental review (consider orthopantomogram), baseline ECG (for patients at risk of arrhythmias).
- **Prior to EACH infusion (at time of presentation to PCH)** – serum or ionised calcium, serum 25-hydroxy vitamin D, UEC, estimated renal clearance, urine beta-hCG (pregnancy test). Serum calcium level must be within normal limit prior to starting the infusion.
- **POST–FIRST infusion (all patients)**:
  - Repeat serum calcium level 24 hours post-infusion and adjust calcium / calcitriol dosing frequencies accordingly.
  - Requirement for serum calcium monitoring on **day 2 and 3 is optional** depending on individual patient's clinical status and is to be determined by the treating consultant.
  - Inpatients may be discharged on day 2 if clinically appropriate. Follow up calcium monitoring may occur in an outpatient setting.
- **POST–SUBSEQUENT infusion (Group 1: patients with risk factors for or history of pamidronate-induced hypocalcaemia)** – monitor as per first infusion.
- **POST–SUBSEQUENT infusion (Group 2: patients with no known risk factors for**

hypocalcaemia):

- Routine serum calcium monitoring is not necessary.

- Ongoing long-term monitoring (annually or as deemed appropriate by treating consultant): dental examination, bone density scan (DXA and pQCT), X-ray.
- Consider yearly analysis of bone turnover markers in patients with osteopenia or osteoporosis – serum P1NP (total procollagen type 1 N-terminal propeptide) and serum CTX (c-terminal telopeptide).

ADVERSE EFFECTS

Acute phase reaction may occur up to 24 – 48 hours after the infusion.[3, 11] Signs and symptoms include low-grade fever, headache, bone pain, chest pain or myalgia.[11]

Common: Acute phase reaction, hypocalcaemia, hypophosphataemia, hypomagnesaemia, hypokalaemia, hypertension, infusion site reaction, headache.[3, 5]

Infrequent: Seizures, sinus tachycardia, atrial fibrillation.[3, 5]

Rare: Osteonecrosis of the jaw or external auditory canal, atypical fractures, anaphylactic shock, angioedema, Stevens-Johnson syndrome, ocular inflammation, renal impairment, heart failure, hypotension, oedema, iritis.[3, 5]

STORAGE[10]

Vial: Store below 25ºC.

Diluted infusion solution: Stable for 24 hours at 2 to 8ºC.

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **pamidronate**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

PCH.MED.Colecalciferol

PCH.MED.Calcium

References

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